

P^ATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 28 May 2001 (28.05.01)	
International application No. PCT/GB00/03424	Applicant's or agent's file reference P23064A/SCR
International filing date (day/month/year) 07 September 2000 (07.09.00)	Priority date (day/month/year) 07 September 1999 (07.09.99)
Applicant GILCHRIST, Thomas et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 05 April 2001 (05.04.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Olivia TEFY Telephone No.: (41-22) 338.83.38
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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P23064A/SCR	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 03424	International filing date (day/month/year) 07/09/2000	(Earliest) Priority Date (day/month/year) 07/09/1999
Applicant GILTECH LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

T/GB 00/03424

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N5/00 A61L27/38 //C03B37/00,C03C3/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C03C A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

MEDLINE, BIOSIS, EPO-Internal, PAJ, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BURNIE J ET AL: "CONTROLLED RELEASE GLASSES (C.R.G.) FOR BIOMEDICAL USES" BIOMATERIALS,GB,ELSEVIER SCIENCE PUBLISHERS BV., BARKING, vol. 2, 1 October 1981 (1981-10-01), pages 244-246, XP000650239 ISSN: 0142-9612	1-7, 12-18
Y	the whole document	8-11,19
X	WO 98 54104 A (HEALY DAVID MICHAEL ;GILTECH LTD (GB); GILCHRIST THOMAS (GB)) 3 December 1998 (1998-12-03) cited in the application	1,4-13, 17-19
Y	abstract page 1, line 17 - line 23 page 4, line 9 - line 21 page 7, line 36 -page 9, line 22 page 17, line 16 - line 21 --- -/--	8-11,19



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

28 March 2001

Date of mailing of the international search report

06/04/2001

Name and mailing address of the ISA

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Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Noë, V

INTERNATIONAL SEARCH REPORT

International Application No

T/GB 00/03424

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 811 302 A (DUCHEYNE PAUL ET AL) 22 September 1998 (1998-09-22) abstract column 1, line 28 - line 30 column 3, line 29 -column 4, line 21 column 8, line 40 -column 11, line 9 -----	1-7,10, 12,14, 15,17,18
A	SALIH, V. ET AL: "The response of human osteoblast cell lines to phosphate-based soluble glasses" BIOCERAM., PROC. INT. SYMP. CERAM. MED. (1998), 11, 269-272 , 1998, XP000990696 the whole document -----	
A	UO MOTOHIRO ET AL: "Properties and cytotoxicity of water soluble Na ₂ O-CaO-P ₂ O ₅ glasses." BIOMATERIALS, vol. 19, no. 24, December 1998 (1998-12), pages 2277-2284, XP004168861 ISSN: 0142-9612 the whole document -----	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/03424

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9854104	A	03-12-1998	AU	7668998 A	30-12-1998
			EP	0988258 A	29-03-2000
US 5811302	A	22-09-1998	US	5643789 A	01-07-1997
			US	5648301 A	15-07-1997
			US	5676720 A	14-10-1997
			CA	2142282 A	03-03-1994
			EP	0672117 A	20-09-1995
			JP	8500248 T	16-01-1996
			WO	9404657 A	03-03-1994

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 March 2001 (15.03.2001)

PCT

(10) International Publication Number
WO 01/18174 A3

- (51) International Patent Classification⁷: C12N 5/00, (74) Agent: MURGITROYD & COMPANY; 373 Scotland Street, Glasgow G5 8QA (GB).
A61L 27/38 // C03B 37/00, C03C 3/16
- (21) International Application Number: PCT/GB00/03424 (81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (22) International Filing Date:
7 September 2000 (07.09.2000)
- (25) Filing Language: English
- (26) Publication Language: English (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- (30) Priority Data:
9920974.4 7 September 1999 (07.09.1999) GB
9927802.0 25 November 1999 (25.11.1999) GB
- (71) Applicant (*for all designated States except US*):
GILTECH LIMITED [GB/GB]; 9/12 North Harbour Estate, Ayr KA8 8AA (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): GILCHRIST, Thomas [GB/GB]; The Lodge, 67 Midton Road, Ayr KA7 2TW (GB). HEALY, David, Michael [IE/GB]; Midton House, By Alloway, Ayr KA7 4EG (GB).
- Published:
— with international search report
- (88) Date of publication of the international search report:
27 September 2001
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: CELL GROWTH SUBSTRATE

(57) Abstract: A cell culture growth substrate comprising a water soluble glass matrix adapted to sustain growth of living cells. Preferably the substrate comprises or is coated with living cells. The water-soluble glass is advantageously phosphate based and comprises glass fibres or finely comminuted particles. The invention also relates to the use of the growth substrate as an implant to replace or promote repair of damaged tissue in a patient and to a method to encourage growth of living tissue.

WO 01/18174 A3



INTERNATIONAL SEARCH REPORT

In ternational Application No

P B 00/03424

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N5/00 A61L27/38 //C03B37/00,C03C3/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C03C A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

MEDLINE, BIOSIS, EPO-Internal, PAJ, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BURNIE J ET AL: "CONTROLLED RELEASE GLASSES (C.R.G.) FOR BIOMEDICAL USES" BIOMATERIALS,GB,ELSEVIER SCIENCE PUBLISHERS BV., BARKING, vol. 2, 1 October 1981 (1981-10-01), pages 244-246, XP000650239 ISSN: 0142-9612	1-7, 12-18
Y	the whole document	8-11,19
X	WO 98 54104 A (HEALY DAVID MICHAEL ;GILTECH LTD (GB); GILCHRIST THOMAS (GB)) 3 December 1998 (1998-12-03) cited in the application	1,4-13, 17-19
Y	abstract page 1, line 17 - line 23 page 4, line 9 - line 21 page 7, line 36 -page 9, line 22 page 17, line 16 - line 21 --- -/-	8-11,19

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

28 March 2001

Date of mailing of the international search report

06/04/2001

Name and mailing address of the ISA

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Authorized officer

Noë, V

INTERNATIONAL SEARCH REPORT

International Application No

P B 00/03424

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 811 302 A (DUCHEYNE PAUL ET AL) 22 September 1998 (1998-09-22) abstract column 1, line 28 - line 30 column 3, line 29 -column 4, line 21 column 8, line 40 -column 11, line 9 -----	1-7, 10, 12, 14, 15, 17, 18
A	SALIH, V. ET AL: "The response of human osteoblast cell lines to phosphate-based soluble glasses" BIOCERAM., PROC. INT. SYMP. CERAM. MED. (1998), 11, 269-272 , 1998, XP000990696 the whole document -----	
A	UO MOTOHIRO ET AL: "Properties and cytotoxicity of water soluble Na ₂ O-CaO-P ₂ O ₅ glasses." BIOMATERIALS, vol. 19, no. 24, December 1998 (1998-12), pages 2277-2284, XP004168861 ISSN: 0142-9612 the whole document -----	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

P B 00/03424

Patent document cited in search report	Publication date	Patent family m mber(s)	Publication date
WO 9854104 A	03-12-1998	AU 7668998 A EP 0988258 A	30-12-1998 29-03-2000
US 5811302 A	22-09-1998	US 5643789 A US 5648301 A US 5676720 A CA 2142282 A EP 0672117 A JP 8500248 T WO 9404657 A	01-07-1997 15-07-1997 14-10-1997 03-03-1994 20-09-1995 16-01-1996 03-03-1994

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)


Applicant's or agent's file reference ./.	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/03424	International filing date (day/month/year) 07/09/2000	Priority date (day/month/year) 07/09/1999
International Patent Classification (IPC) or national classification and IPC C12N5/00		
Applicant GILTECH LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
 - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 05/04/2001	Date of completion of this report 04.12.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Trommsdorff, M Telephone No. +49 89 2399 7361



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/03424

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-41 as originally filed

Claims, No.:

1-19 as originally filed

Drawings, sheets:

1/23-23/23 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03424

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims
	No: Claims 1-19
Inventive step (IS)	Yes: Claims
	No: Claims 1-19
Industrial applicability (IA)	Yes: Claims 1-17
	No: Claims 18, 19: no opinion

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

1. Cited documents

The following documents (D) are referred to in this communication; the numbering is the same as in the search report and will be adhered to in the rest of the procedure:

- D1: BURNIE J ET AL: 'CONTROLLED RELEASE GLASSES (C.R.G.) FOR BIOMEDICAL USES' BIOMATERIALS, GB, ELSEVIER SCIENCE PUBLISHERS BV., BARKING, vol. 2, 1 October 1981 (1981-10-01), p.244-46 ISSN: 0142-9612
- D2: WO 98 54104 A (HEALY DAVID MICHAEL; GILTECH LTD (GB); GILCHRIST THOMAS (GB)) 3 December 1998 (1998-12-03) cited in the application
- D4: SALIH, V. ET AL: 'The response of human osteoblast cell lines to phosphate-based soluble glasses' BIOCERAM., PROC. INT. SYMP. CERAM. MED. 11, p.269-72, 1998
- D5: UO MOTOHIRO ET AL: 'Properties and cytotoxicity of water soluble Na_2O - CaO - P_2O_5 glasses.' BIOMATERIALS, vol.19, no.24, Dec 1998, p.2277-84 ISSN:0142-9612

2. Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 2.1. The claims are directed to a cell culture growth substrate comprising a soluble glass matrix adapted to sustain growth of living cells and to the use of said substrate for promoting cell growth.

A number of documents disclose controlled release glasses (CRG) for biomedical uses.

In D1 different CRG containing phosphorous pentoxide (P_2O_5) and oxide forms of calcium and sodium are tested in monolayer cell culture and shown not to affect cell growth (p.245, 1st paragraph). Implants of CRG rods in sheep are also well accepted by the host and provoke only a very mild non-specific inflammation reaction (p.245, 2nd paragraph).

Hence, the water soluble glass matrix and the methods of use described in D1 contain all the technical features of claims 1-7 and 12-18. Thus, D1 is novelty destroying to the subject-matter of said claims (Art. 33(1) and (2) PCT).

D2 describes different water soluble glass fibres containing phosphorous pentoxide as the glass former, alkali metals, lanthanoid oxides or carbonates as glass modifiers and boron as glass additive and having a dissolution rate of 0.01-2 mg/cm²/h at 38°C (p.7, l.36-p.9, l.22). Several examples of such glass fibres are given (see examples 1-15). The fibres of examples 11 are suitable for biodegradable applications, those of example 15 are further specified to be suitable for orthopaedic implants and tissue engineering applications (p.17, l.16-21). Said glass is also shown to allow a controlled release of metal ions such as silver ions (p.9, l.8-22).

Consequently, the fibres disclosed in D2 are suitable for use in cell culture. Therefore, the teaching of D2 is prejudicial to the novelty of the subject-matter of claims 1 and 4-13 and 19 (Art. 33(2) PCT).

2.2. Following relevant documents will only be discussed briefly:

In D4 phosphate-based soluble glasses are tested and shown to be not cytotoxic for human osteoblasts.

D5 also analyses the cytotoxicity of different water soluble Na₂O-CaO-P₂O₅ glasses depending on their P₂O₅ and CaO content.

2.3. Claims 18 and 19 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

2.4. The subject-matter of claims 1-17 is industrially applicable in the field of pharmaceutical industry (Art. 33(4) PCT).

3. Re Item VII

Certain defects in the international application

3.1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1 is not mentioned in the description, nor is this document identified therein.

4. Reason VIII

Certain observations on the international application

- 4.1. Claim 1 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved, i.e. to sustain growth of living cells, which merely amounts to a statement of the underlying problem. Indeed, substrates comprising a water soluble glass matrix are state of the art. The technical features necessary for said substrates to achieve this result thus should be added. Moreover, it would appear that it is an inherent feature of any cell culture growth substrate to sustain cell growth.